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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
HAYES, ROBERT CLINTON	
ART UNIT	**PAPER NUMBER**
1647	

DATE MAILED: 03/18/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/821,831	BARTLETT ET AL.	
	Examiner	Art Unit	
	Robert C. Hayes, Ph.D.	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 January 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-30* is/are pending in the application.

4a) Of the above claim(s) *8-12,14 and 18-30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,13 and 15-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-30* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *7/16/01 & 3/13/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Sequence Compliance

1. Page v of amendment 7/21/01 no longer lists the arrows indicating the amino acid conversions on line 7, nor correctly lists page 35 (versus pg. 25) on line 9 for amendment. "SEQ ID NO:9, SEQ ID NO:10" on line 15 is also incorrectly bracketed. Nonelected claim 11 must also be amended to recite a SEQ ID NO, in order to be in compliance with the Sequence Rules. Alternatively, claim 11 could be cancelled to obviate this objection.

Election/Restriction

2. Applicant's election of Group I in Paper No. 1/5/04 (i.e., as it relates to rat SEQ ID NO:3) is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 8-12, 14 & 18-30 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 1/5/04. For example, SEQ ID NO: 7 is not contained within SEQ ID NO: 3 (i.e., as it relates to claims 10-12), and SEQ ID NO:3 is not of "human, primate or murine origin" (i.e., as it relates to claim 8).

Claim Rejections - 35 U.S.C. § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 1-7, 13 & 15-17 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The instant specification describes the human p75/LNGFR cDNA molecule of SEQ ID NO: 1 and the rat p75/LNGFR cDNA molecule of SEQ ID NO: 3. Page 15 of the specification then states that "[t]he nucleic acid molecule of the present invention may be based on a nucleotide sequence of the gene or cDNA encoding p75NTR from any animal such as from mammals. Preferred mammals include human, primates, livestock animals (e.g., cows, sheep, horses, pigs, donkeys, goats), laboratory test animals, (e.g., rabbits, mice, rats, guinea pigs, hamsters), companion animals (e.g., dogs, cats) and captive wild animals)." In contrast, no written description of any LNGFR (p75NTR) nucleic acid molecules from any of these other mammals are described. Nor is any written description provided for any "gene" sequences from any species, which is distinct from the human and rat cDNA sequences of SEQ ID NOs: 1 & 3, respectively, versus that stated on pages 12 & 13 of the specification. Nor are any "*other* ligand-binding molecules" adequately described on page 12 of the specification (i.e., as it relates to generic claim 5). Likewise, no allelic variants that are 60% identical, or that putatively

hybridize, to SEQ ID NO: 3 (i.e., as it relates to claim 13) are adequately described by nucleotide sequence within the instant specification by which the skilled artisan could reasonably visualize such at the time of filing Applicants' application. Thus, the written description requirements under 35 U.S.C. 112, first paragraph, are clearly not met by the current claims.

It is suggested that amending the claims to a nucleic acid molecule comprising or consisting of SEQ ID NO: 3 should obviate this particular rejection. See MPEP 2163.

4. Claims 1-7, 13 & 15-17 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the specific disclosed nucleotide sequence of SEQ ID NO: 3 encoding the rat p75/LNGF receptor, does not reasonably provide enablement for any structurally and functional uncharacterized nucleic acid molecules or functional equivalents, derivatives, or homologues thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The name "nucleotides which encode an amino acid sequence which is capable of signalling (*sic*), inducing or otherwise facilitating the death of a cell", or "functional equivalent, derivative, homologue thereof", or "nucleotide substitutions, insertions, deletions, or rearrangements" thereof (e.g., as defined on pages 13-16 of the specification) sets forth no structural and little functional characteristics. In contrast, the specification fails to define what critical nucleotide residues encode any putative amino acid sequence putatively "capable of signaling, inducing or otherwise facilitating the death of a cell", as it relates to SEQ ID NO: 3. Nor does the instant specification teach how to distinguish any such randomly substituted,

inserted, deleted, or rearranged nucleic acid-related molecule/ biologically functional equivalent from any different nucleic acid molecule that possesses none of the desired functions of the instant invention. In contrast, the skilled artisan would reasonably expect that any such random mutation, substitution, insertion, deletion, or rearrangement to the nucleic acid encoding the rat LNGFR molecule of SEQ ID NO: 3 would result in a polynucleotide encoding an inactive protein. For example, Rudinger states on page 3 that "it is impossible to attach a unique significance to any residue in a sequence. A given amino acid will not by any means have the same significance in different peptide sequences, or even in different positions of the same sequence." Rudinger further states on page 6 that "the significance of particular amino acid sequences for different aspects of biological activity cannot be predicted *a priori* but must be determined from case to case by painstaking experimental study." Therefore, the lack of guidance provided in the specification, as to what minimal structural requirements are necessary for a nucleic acid to encode a functional polypeptide molecule, would prevent the skilled artisan from determining whether any random mutation/substitution/insertion/deletion/rearrangement to the rat nucleic acid molecule of SEQ ID NO: 3 could be made that retains the desired function of the instant invention, because any such polynucleotide would be expected by to encode proteins that have adversely altered their biologically active 3-dimensional conformation without requiring undue experimentation to determine otherwise.

5. Claims 1-7, 13 & 15-17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Since it is the sense strand that encodes a polypeptide, versus the noncoding antisense strand/ complementary strand, the claims are indefinite, as currently recited for "or complementary sequence… which encodes" (i.e., as it relates to claim 1). Likewise, "hybridizing thereto" would alternatively require hybridizing to the "fully complementary strand" of the nucleotide molecule, in order to generate a polynucleotide molecule that encodes a functional polypeptide (i.e., as it relates to claim 15).

In addition, it is ambiguous how an "amino acid *sequence*" is envisioned to be "adjacent, proximal or otherwise juxtaposed to [a] membrane", or how an "amino acid", versus polypeptide, can be "in multimeric form", or "a soluble form" (i.e., as it relates to claims 1 & 7).

6. Claims 7 & 13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 7 & 13 are indefinite due to the recitations of "wherein said amino acid sequence is a soluble form of the p75NTR receptor *corresponding to an intracellular region adjacent…* " or for "comprises a sequence of nucleotides which *corresponds*… to a death signal region". In other words, nucleotides alternatively *encode* amino acid residues of a death signal region or encode amino acid residues of an intracellular region of a polypeptide. Moreover, an "intracellular region", versus extracellular region, is not reasonably the "soluble" region of a receptor; thereby, making claim 7 further confusing.

Lastly, the recitation of "*substantially* as set forth in SEQ ID NO: 3" in claim 13 is indefinite because it is unknown what metes and bounds define when a sequence is, or is no longer, "substantially" similar; for this otherwise relative term.

Claim Rejections - 35 U.S.C. § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-7, 13 & 15-17 are rejected under 35 U.S.C. 102(b) as being anticipated by Radeke et al (1987; IDS Ref # AR).

Radeke et al. teach the rat p75 NGF receptor cDNA sequence which comprises SEQ ID NO: 3 (pg. 596; Fig. 5; as it relates to claim 13), and therefore, also anticipates all limitations related to "hybridizing", "about 60% identity thereto", "a homologue, analogue or derivative" thereof, or "*comprises* all or a part of the cytoplasmic domain" for this cytokine receptor protein that *comprises* an extracellular ligand-binding domain and a transmembrane domain ,or *comprises* "an intracellular region…" (i.e., as it relates to claims 1-7 & 13). Radeke et al. further disclose the extracellular portion of their receptor (i.e., the "soluble form"; Fig. 5; as it relates to claim 7). In that Radeke et al. teach gene constructs/vectors (i.e., pUC9 and pcDL1), in which the pUC9 or pcDL1 vector promoter sequences are inherently and operably connected to the inserted p75 NGF receptor "sequence of nucleotides" followed by terminator sequences

(pgs. 594-595; due to the position of the multicloning sites in these vectors), the limitations of claims 15-17 are also met.

It is suggested that amending claims 15-17 to "an expression vector comprising the nucleotide sequence of SEQ ID NO: 3" would reflect more conventional claim language.

Conclusion

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Robert Hayes whose telephone number is (57) 272-0885. The examiner can normally be reached on Monday through Thursday, and alternate Fridays, from 8:30 AM to 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz, can be reached on (571) 272-0887. The fax phone number for this Group is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Robert C. Hayes, Ph.D.
March 16, 2004
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